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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,735	ROBERTS ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-47* is/are pending in the application.

4a) Of the above claim(s) *11,12 and 15-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-10, 13-14 and 46-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. The previous Final rejection mailed on 9/24/04 is hereby vacated. The new Final is set forth below. Examiner apologized for any inconveniences.

2. Applicant's amendment, filed 8/21/04, is acknowledged.

3. Claims 1-5, 7-47 are pending.

4. Claims 11-12 and 15-45 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

5. In view the exclusion of SEQ ID NO: 54 based on the art rejection, the Examiner has extended the search to cover SEQ ID NO: 53.

6. Claims 1-5, 7-10, 13-14 and 46-47 are under consideration in the instant application. as they read on a peptide comprising the sequence R_1-X_1-X_2-X_3-X_4-R_2 and compositions thereof, SEQ ID NOs: 51 and 53.

7. Applicant argument regarding the restriction that claims 11-12 and 15-19 have been amended to be dependent from claim 1 and that they are all directed to combinations comprising the subcombination of the peptides of claim 1, is acknowledged but the restriction requirements deemed Final for the reasons off record. Further, Inventions of Group I and Group II are related as mutually exclusive species in an intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than the final product (MPEP § 806.04(b), 3rd paragraph), and the species are patentably distinct (MPEP § 806.04(h)). In the instant case, the intermediate product is deemed to be useful as antigen and the inventions are deemed patentably distinct since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

8. Claim 46 is objected to under 37CFR 1.821(d) for failing to recite the SEQ ID NOS. in the claims. Applicant is reminded of the sequence rules which require a submission for all sequences of 10 or more nucleotides or 4 or more amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

9. In view of the amendment filed on 8/21/04, the rejections are set forth below.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 2, 5 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 2 and 9 are indefinite for reciting "from about 4 amino acids to about 12 amino acids" in line 1. It is unclear how many amino acids constitute "about". One of skill in the art would not know if applicant meant 3 amino acid, as many as 13 amino acids, or even more.

B. The "X1-X2-X3-X4" recited in claim 5 lacks antecedent basis in base claim 1. Base claim 1 only recites "R1-X1-V-R-X4-R2".

Applicant's arguments, filed 8/21/04, have been fully considered, but have not been found convincing.

Applicant traverses the rejection because it fails to present a prima facie case of indefiniteness in light of the standard set forth at MPEP 2173.05(b). Applicant submits that the "term" is not indefinite. Applicant submits that the skilled person would understand that the number of amino acid can only be an integer such that the term "about 4 amino acids" would not be so ambiguous allegation posed in the statement of the rejection. Applicant further submits that the skilled person would certainly recognize "about 4 amino acids" to include 3 amino acids as well as 5 amino acids because the language would be understood as not limited to only "4 amino acids", and that "about 12 amino acids" to include 11 amino acids as well as 13 amino acids because the language would understood as not limited to only "12 amino acids". Applicant points out that the Examiner interpreted the term about 12 amino acids to encompass a length of 14 amino acids. which indicate the lack of ambiguity with respect to the scope.

Contrary to applicant argument the term about when used with amino acid length and/or range is ambiguous because it is unclear what is the upper or lower limits of the amino acids claimed. Would a 20, 25, 30 or 50 amino acid sequence still reads on the scope of about 12 amino acids.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-5, 7-10, 13-14 and 46-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide consisting of SEQ ID NOs: 19, 22 and 24-32 or their full retro-inverso peptide sequence, does not reasonably provide **enablement** for any

peptide "comprising" the sequence R1-X1-V-R-X4-R2 in claim 1, wherein R1 is a peptide "comprising" SEQ ID NO:13-17 in claim 3, or wherein the peptide "comprising" "at least one sequence" of SEQ ID NO:18-32 in claim 4, wherein the peptide is "partial retro-inverso peptide sequence in claim 6, that comprises "at least one D-amino acid" in claim 7, a retro-inverso synthetic peptide "comprising" the amino acid sequence in claim 8, the peptide of claim 6 "comprising" the sequence of SEQ ID NO: 25 in claim 10, or a pharmaceutical composition comprising a peptide and pharmaceutical acceptable carrier of claim 13, or a sterile composition comprising a peptide and a sterile aqueous solution of claim 14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 5/21/04.

Applicant's arguments, filed 8/21/04, have been fully considered, but have not been found convincing.

Applicant stated that reliance on assertions of unpredictability are not enough to doubt the presumption of an enabling disclosure. Applicant contends that there must be objective reasons why undue experimentation is necessary to make and use the claimed invention. Further, undue experimentation is not the same as the absence of experimentation. Applicant submits that the disclosure and the claims were enabling as originally filed for the full scope of the claims because no adequate and objective reasons have been presented to doubt the ability to make and use peptides and compositions as encompassed by the claims and described in the specification. Applicant submits that the focus of the rejection on the lack of sufficient guidance and predictability in determining which modifications would lead to the inhibition of $\alpha 3\beta 1$/TSP1 interaction is misplaced. Applicant argues that the rejection presumes a requirement for absolute predictability as to which peptides will or will not have the functionalities as disclosed by the instant application and such is not appropriate standard. Applicant submits that the standard is that of whether undue experimentation is required to make and use the claimed invention. Applicant further submits that a skilled person would be able to make a wide range of peptides, all of which comprise the sequence as recited in the claims and disclosed as the instant invention, and then identify their ability to function in the various activities disclosed in the instant application by using only routine and repetitive experimentation. Applicant argues that a skilled person can make various peptides and compositions as encompassed by the claims and then use only routine and repetitive screening as "experimentation" to identify those that possess the functionalities as disclosed in the instant application. Applicant points out the rejection attempts to support its position by asserting generalities relating to the concept of altered protein structures leading to altered functionalities. Applicant submits that the assertions are irrelevant if no undue experimentation is needed to identify and use peptides as encompassed by the invention. Applicant submits that methods for such identification include those disclosed in the instant application and known to the skilled person.

However, In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Applicant has provided little or no

guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the peptide which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Due to the large quantity of experimentation necessary to obtain the peptide variants, to generate the infinite number of derivatives recited in the claims, and to determine the specific activity of the infinite variants, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes that biological activity cannot be predicted based on structural similarity, and the breadth of the claims which embrace a broad class of structural variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. Identification of peptide sequences that inhibits the interaction between $\alpha 3\beta 1$/TSP1 using only routine and repetitive experimentation is not sufficient to enable the claimed invention. However, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and use the invention, not how to screen to identify the invention. Until the time such peptide sequences identity are found, then one skill in the art can make them.

Applicant submits that contends that the rejection base on that the disclosures of peptid3es comprising at least one, but not all, D-amino acids is also misplaced. Applicant submits that there is no objective reasons have been provided as to why a skilled person would be unable to make, identify, and use peptide without undue experimentation. Applicant states that sufficiency of enablement does not require absolute predictability as to the possible positions of all D-amino acids.

However, has been clearly stated in the previous office action that one skilled in the art at the time of the invention would not be able to predict which amino acid(s) of the peptide can be D-amino acid and still provide inhibition of $\alpha 3\beta 1$/TSP1 interaction. Consequently the skilled artisan would not know how to make the instant invention as broadly claimed.

Regarding the pharmaceutical/sterile composition, Applicant argues that there is no objective reasons to doubt the statements in the instant application regarding the uses of the compositions as disclosed and claimed. Applicant further argues that in the absence of reasons to undue levels of unpredictability in formulating and testing the compositions as claimed, the claimed compositions must be presumed enabled.

However, if the use disclosed is of such nature that the art is unaware of successful treatments with chemically analogous compounds, a more complete statement of how to use must be supplied. There must be a rigorous correlation of pharmacological activity between the disclosed in vitro method and an in vivo method to establish practical use. "First, although appellants' specification describes certain in vitro experiments, there is no correlation on this record between in vitro experiments and a practical utility in currently available form for humans or animals. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art

has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to utility in humans or animals" (emphasis added). Ex parte Maas, 9 USPQ2d 1746. "There is no evidence of record that experimental animal models have been developed in this area which would be predictive of human efficacy." Ex parte Balzarini, 21 USPQ2d 1892.

14. Claims 1-5, 7-10, 13-14 and 46-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 5/21/04.

Applicant's arguments, filed 8/21/04, have been fully considered, but have not been found convincing.

Applicant traverses that rejection base on the ground that no *prima facie* case of an inadequate written description has been presented. Applicant submits that there is no difficulty with "envisioning" or even writing down all the sequences encompassed by the claims. Applicant submits that the formula is given, and the peptides are clearly those having a definite number of sequence possibilities. Applicant submits that such sequence possibilities are present in every peptide encompassed by the claims, and so there is no factual basis to support the instant rejection's assertion of inabilities by the skilled person. Applicant points out the very structures defined by the formula recited in the claims are the structures which have been disclosed as having functional properties in the instant application. Applicant submits that each of the sequence possibilities encompassed by the formula is a representative species supporting the scope of the claims. Applicants submit that they are in possession of the claimed invention. Applicant posses the following question for consideration: does the instant application place the invention as claimed in the possession of a skilled artisan presented with the instant disclosure? Can that artisan practice the claimed invention? Applicant submits that no basis has been presented for why the skilled person cannot follow the instant disclosure to make and use all the peptides encompassed by the claims.

However, there is no described or art-recognized correlation or relationship between the structure of the invention, the generic formulae and it's anti-angiogenic, anti-proliferation function (i.e., inhibition of $\alpha 3\beta 1$/TSP1 interaction), the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants which retain the features essential to the instant invention.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prater et al, Miles et al, WO 92/09628 or U.S. Patent No. 6,020,312 in view of U.S. Patent NO. 5,770,563 (all of record).

Parater et al teach a 19 amino acid peptide comprising the sequence QVRI (see page 1031, Figure 8, under P.Falciparum C.S. protein in particular), wherein X1 is Q, X2 is V, X3 is R and X4 is I, wherein R1 is a peptide of 1-6 amino acids, and R2 is one amino acid. The term "comprising" in instant claim 1 is open ended. It would open up the claim to include the reference 19 amino acid sequence.

Miles el al teach peptides comprising DLRL and are 14 amino acid in length (see page 30943, Tables I and II in particular), wherein X1 is D, X2 is L, X3 is R and X4 is L, wherein R1 is a peptide of 5 amino acids, and R2 is a peptide of 1-3 amino acid. Miles et al further teach a peptide that is all D-amino acid (see table II, 2nd sequence in particular). Miles et al further teach that the peptides were dissolved in 1 ml of DMS/water (1:9), and diluted to desired concentrations with PBS (see page 30940, 2nd col., under cell adhesion in particular). PBS is considered to be a pharmaceutically acceptable carrier. The term "comprising" in instant claim 1 is open ended. It would open up the claim to include the reference 14 amino acid sequence.

The `628 publication teaches the a 6 amino acid peptide comprising the sequence DVRF (claimed SEQ ID NO: 54) (see page 36, line 15, published claim 10 in particular), wherein X1 is D, X2 is V, X3 is R and X4 is F, wherein R1 is one amino acid, and R2 is one amino acid. The `628 publication teaches that the peptide contain at least one D-amino acid (see published claim 1 in particular). The `628 publication further teaches a composition having the peptide **KDVRF**E (see published claim 17, page 43 in particular).

The `312 patent teaches the a 6 amino acid peptide comprising the sequence SLRF (see col. 39, SEQ ID NO:19, in particular), wherein X1 is S, X2 is L, X3 is R and X4 is F, wherein R1 is 2 amino acids, and R2 is a hydroxide/amide (see col., 25, under Example XIII in particular) The `312 patent teaches that the peptide contain one or two D-amino acids (see col., 5, lines 52-54, in particular). The `312 patent further saline solutions, pharmaceutically acceptable buffers and solvents and the like may also be utilized as carriers for the peptide compositions of the invention (see col. 7, lines 65-67 in particular).

The claimed invention differs from the reference teachings only by the recitation of a retro-inverso synthetic peptide and all amino acids are D-amino acids in 8.

The `563 patent teaches thrombospondin peptides which all D-amino acid peptide analog of a peptide from the A chain of the extracellular matrix protein laminin replicated the activity of the natural sequence to influence tumor cell adhesion and growth in vitro and in vivo (page 255-258 in particular). The `563 patent further teaches that retro-inverso peptides have been successfully applied to increase the stability and biological activity of peptide sequences for therapeutic applicantions. Finally, the `563 patent teaches that the peptides may be modified to include full or partial retro-inverso sequences. Use of retro-inverso peptide sequences minimizes enzymatic degradation and, therefore, extends biological half-life of the peptide moiety (see col., 25-55, in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the amino acids of the peptide taught by the Prater et al, Miles et al, WO 92/09628 or U.S. Patent No. 6,020,312 full or partial retro-inverso sequences as taught by `563 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because use of retro-inverso peptide sequences minimizes enzymatic degradation and, therefore, extends biological half-life of the peptide moiety as taught by the `563 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 1-3, 5, 7, 13-14 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The sequence "R_1-X_1-V-R-X_4-R_2" claimed in claim 1, line 2 and the sequence "R_1-D-V-R-F-R_2, or partial or full retro-inverso sequences thereof, wherein R1 is a hydrogen or a peptide of 1 to 6 amino acids, an acyl or an aryl group; and R2 is a peptide of 2 or 3 amino acids, a hydroxide or an amide" claimed in claim 46, lines1-3 represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 8/21/04 does not point to the specification for support for the newly added limitation "R_1-X_1-V-R-X_4-R_2" as claimed in claim 1 and "R_1-D-V-R-F-R_2, or partial or full retro-inverso sequences thereof, wherein R1 is a hydrogen or a peptide of 1 to 6 amino acids, an acyl or an aryl group; and R2 is a peptide of 2 or 3 amino acids, a hydroxide or an amide" claimed in claim 46. However, the specification does not provide a clear support of "R_1-X_1-V-R-X_4-R_2" and "R_1-D-V-R-F-R_2". While the specification discloses the sequence R_1-X_1-X_2-X_3-X_4-R_2, wherein X1 is N, Q, D or S, X2 is V, I or L, X3 is R or K, X4 is V, I, L or F. Applicant is creating a new subgenus of peptides. A subgenus is not necessarily implicitly described by a genus encompassing it and a species upon which it reads, see *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972). The instant claim now recites a limitation which was not clearly disclosed in the specification and recited in the claims as originally filed.

Obviousness is not the standard for the addition of new limitations to the disclosure as filed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). New Matter is a written description issue.

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

21. Claims 1-2, 5 and 13-14 are rejected under 35 U.S.C. 102(a) as being anticipated by JP10-25896 (9/1998) (of record).

The '896 publication teaches the a 9 amino acid peptide comprising the sequence QVRF (claimed SEQ ID NO: 53) (see page 10, the table, 2nd peptide in particular), wherein X1 is Q and X4 is F, wherein R1 is one amino acid, and R2 is 1-3 amino acids. The term "comprising" would open the claimed peptide to include the extra amino acid(s) at the C-terminal.

The reference teachings anticipate the claimed invention.

22. Claims 1-2 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat. No. 5,789,184 (of record).

The `184 patent teaches the a 11 amino acid peptide comprising the sequence QVRF (claimed SEQ ID NO: 53) (see page 123, patented SEQ ID NO: 55 in particular), wherein X1 is Q and X4 is F, wherein R1 is 1-3 amino acids, and R2 is 1-3 amino acids. The term "comprising" would open the claimed peptide to include the extra amino acid(s) at the C-terminal. The `184 patent teaches the peptides in solution (see col., 7 line 5 and line 10 in particular).

The reference teachings anticipate the claimed invention.

23. Claims 7-9 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP10-25896 or US Pat. No. 5,789,184 each in view of U.S. Patent NO. 5,770,563 (all of record).

The teachings of JP10-25896 publication and US Pat. No. 5,789,184 have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of Partial and full retro-inverso peptide sequences in claim 6, at least one D-amino acid in claim 7, all amino acids are D-amino acids in 8, a sterile/pharmaceutical composition in claims 13-14.

The `563 patent teaches thrombospondin peptides which all D-amino acid peptide analog of a peptide from the A chain of the extracellular matrix protein laminin replicated the activity of the natural sequence to influence tumor cell adhesion and growth in vitro and in vivo (page 255-258 in particular). The `563 patent further teaches that retro-inverso peptides have been successfully applied to increase the stability and biological activity of peptide sequences for therapeutic applications. Finally, the `563 patent teaches that the peptides may be modified to include full or partial retro-inverso sequences. Use of retro-inverso peptide sequences minimizes enzymatic degradation and, therefore, extends biological half-life of the peptide moiety (see col., 25-55, in particular). Moreover, the `563 patent teach a pharmaceutical composition according to the invention, wherein the composition comprises an effective amount of a peptide and the sequences set forth in Table 3, in combination with a pharmaceutically acceptable excipient or carrier for the use in treatment of the particular disorder for which treatment is sought (see col., 33-34 under Pharmaceutical Compositions in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the amino acids of the peptide taught by the Prater et al full or partial retro-inverso sequences as taught by `896 publication or `184 patent and to include them in a pharmaceutical (sterile) composition.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because use of retro-inverso peptide sequences minimizes enzymatic degradation and, therefore, extends biological half-life of the peptide moiety as taught by the `563 patent. Further

because the composition can be use in treatment of the particular disorder for which treatment is sought.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

24. No claim is allowed.

25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
March 10, 2005

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